

## PATENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner  
US Department of Commerce  
United States Patent and Trademark  
Office, PCT  
2011 South Clark Place Room  
CP2/5C24  
Arlington, VA 22202  
ETATS-UNIS D'AMERIQUE  
in its capacity as elected Office

<b>Date of mailing</b> (day/month/year) 11 January 2001 (11.01.01)	
<b>International application No.</b> PCT/US00/06940	<b>Applicant's or agent's file reference</b> 2370-56
<b>International filing date</b> (day/month/year) 17 March 2000 (17.03.00)	<b>Priority date</b> (day/month/year) 18 March 1999 (18.03.99)
<b>Applicant</b> MAJOR, Eugene, O. et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:  
13 September 2000 (13.09.00)

☐ in a notice effecting later election filed with the International Bureau on:  
\_\_\_\_\_

2. The election ☒ was  
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

<b>The International Bureau of WIPO</b> 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	<b>Authorized officer</b> Juan Cruz Telephone No.: (41-22) 338.83.38
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# PATENT COOPERATION TREATY

From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

## PCT

### WRITTEN OPINION

(PCT Rule 66)

To: B.J. SADOFF  
NIXON & VANDERHYE P.C.  
1100 NORTH GLEBE ROAD, 8TH FLOOR  
ARLINGTON, VIRGINIA 22201-4714

Date of Mailing  
(day/month/year)

11 OCT-2001

Applicant's or agent's file reference  
2370-56

REPLY DUE within ONE months  
from the above date of mailing

International application No.  
PCT/US00/06940

International filing date (day/month/year)  
17 MARCH 2000

Priority date (day/month/year)  
18 MARCH 1999

International Patent Classification (IPC) or both national classification and IPC  
IPC(7): C12N 05/06, 05/08 and US Cl.: 435/325, 368

Applicant  
PRO-VIRUS, INC.

1. This written opinion is the first (first, etc.) drawn by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:

- I ☒ Basis of the opinion
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step or industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

3. The applicant is hereby invited to reply to this opinion.

**When?** See the time limit indicated above. ~~The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).~~

**How?** By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

**Also** For an additional opportunity to submit amendments, see Rule 66.4.  
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 *bis*.  
For an informal communication with the examiner, see Rule 66.6.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 18 JULY 2001

Name and mailing address of the IPEA/US  
Commissioner of Patents and Trademarks  
Box PCT  
Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized officer

*Robert C. Hayes*  
ROBERT C. HAYES, Ph.D.

Telephone No. (703) 308-0196

WRITTEN OPINION

International application No.

PCT/US00/06940

**I. Basis of the opinion**

1. With regard to the **elements** of the international application: \*

☒ the international application as originally filed

☒ the description:

pages 1-51 , as originally filed  
pages NONE , filed with the demand  
pages NONE , filed with the letter of \_\_\_\_\_

☒ the claims:

pages 52-55 , as originally filed  
pages NONE , as amended (together with any statement) under Article 19  
pages NONE , filed with the demand  
pages NONE , filed with the letter of \_\_\_\_\_

☒ the drawings:

pages 1-3 , as originally filed  
pages NONE , filed with the demand  
pages NONE , filed with the letter of \_\_\_\_\_

☒ the sequence listing part of the description:

pages NONE , as originally filed  
pages NONE , filed with the demand  
pages NONE , filed with the letter of \_\_\_\_\_

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.  
These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).  
☐ the language of publication of the international application (under Rule 48.3(b)).  
☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the written opinion was drawn on the basis of the sequence listing:

- ☐ contained in the international application in printed form.  
☐ filed together with the international application in computer readable form.  
☐ furnished subsequently to this Authority in written form.  
☐ furnished subsequently to this Authority in computer readable form.  
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.  
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☒ The amendments have resulted in the cancellation of:

- ☒ the description, pages NONE  
☒ the claims, Nos. NONE  
☒ the drawings, sheets/fig NONE

5. ☐ This opinion has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c))

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed".

WRITTEN OPINION

International application No.  
PCT/US00/06940

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been and will not be examined in respect of:

☐ the entire international application.

☒ claims Nos. 5-11, 14-25 and 29-32

because:

☐ the said international application, or the said claim Nos. \_ relate to the following subject matter which does not require international preliminary examination (*specify*).

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. \_ are so unclear that no meaningful opinion could be formed (*specify*).

☐ the claims, or said claims Nos. \_ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. (See Attached).

2. A written opinion cannot be drawn due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

WRITTEN OPINION

International application No.

PCT/US00/06940

**V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. statement

Novelty (N)	Claims	<u>NONE</u>	YES
	Claims	<u>1-4, 12-13, 26-28 &amp; 33-34</u>	NO
Inventive Step (IS)	Claims	<u>NONE</u>	YES
	Claims	<u>1-4, 12-13, 26-28 &amp; 33-34</u>	NO
Industrial Applicability (IA)	Claims	<u>1-4, 12-13, 26-28 &amp; 33-34</u>	YES
	Claims	<u>NONE</u>	NO

2. citations and explanations

Claims 1-4, 12-13, 26-28 and 33-34 lack novelty under PCT Article 33(2) as being anticipated by Major et al.

Major et al disclose isolated, immortalized human fetal neuro-derived cell lines, which "generally produce progenitor neuronal and glial cells"; thereby, being multipotent, by definition (e.g., column 7, lines 22-37; as it relates to claims 1-3, 12 and 33). Cells derived from SVG cells are also described by Major (e.g., column 4, lines 66 - column 5, line 1; column 7, lines 57-65), which further appear identical to those cells (i.e., multipotent cells) described on pages 18 and 20 of the instant description (i.e., as it also relates to claims 1-3, 12 and 33). In that all of these cells described by Major et al reasonably appear identical to the alternative names of "NG1, NG2 and NG3" cells recited in claim 13, and inherently express markers that uniquely define what constitutes a multipotent stem cell, the limitations of claims 4 and 13 are met; absent evidence to the contrary. Finally, in that the process of producing multipotent neural stem cells does not materially change the multipotent neural stem cell product produced, the limitations of claims 26-28 and 34 are anticipated.

Claims 1-4, 12-13, 26-28 and 33-34 lack novelty under PCT Article 33(2) as being anticipated by Weiss et al.

Weiss et al disclose isolated human multipotent neuro-derived cell lines (i.e., neurospheres; as it relates to claims 33-34), which are clonally-derived/"immortalized" and have the "potential to differentiate toward a neuronal cell or a glial cell" (e.g., column 11, lines 49-56; columns 13, 17-18, 21-22, 36 and 48; as it relates to claims 1-3 and 12). In that the multipotent stem cells described by Weiss et al reasonably appear identical to the alternative names of "NG1, NG2 and NG3" cells recited in claim 13, and inherently express markers that uniquely define what constitutes a multipotent stem cell (e.g., column 56), the limitations of claims 4 and 13 are met; absent evidence to the contrary. Finally, in that the process of producing multipotent neural stem cells does not materially change the multipotent neural stem cell product produced, the limitations of (Continued on Supplemental Sheet.)

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US00/06940

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C12N 05/06, 05/08

US CL : 435/325, 368

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/325, 368

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

MEDLINE, BIOSIS, USPATFULL

search terms: multipotent, stem, CNS, neur####, immortal, SVG, neurosphere, A2B5, TnTx, ChTx, nestin, NG#

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5,753,491 A (MAJOR et al) 19 May 1998, cols. 3-4, 6-8, 12, 14-15, 17-18 & 20-22.	1-4, 12-13, 26-28 & 33-34
X --- A	US 5,750,376 A (WEISS et al) 12 May 1998, cols. 10-12, 15-20, 30-42 & 55-61.	1-4, 12, 26-28 & 33-34 ----- 13

☐ Further documents are listed in the continuation of Box C.☐ See patent family annex.

* Special categories of cited documents:	*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
*A* document defining the general state of the art which is not considered to be of particular relevance	*X* document of particular relevance, the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
*E* earlier document published on or after the international filing date	*Y* document of particular relevance, the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
*L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*G* document member of the same patent family
*O* document referring to an oral disclosure, use, exhibition or other means	
*P* document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

05 JULY 2000

Date of mailing of the international search report

11 AUG 2000

Name and mailing address of the ISA/US  
Commissioner of Patents and Trademarks  
Box PCT  
Washington, D.C. 20231

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# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US00/06940

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

Please See Extra Sheet.

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  
1-4, 12-13, 26-28 & 33-34

Remark on Protest

☐

The additional search fees were accompanied by the applicant's protest.

☐

No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US00/06940

## BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING

This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

- Group I, claim(s) 1-4, 12-13, 26-28 and 33-34, drawn to an isolated immortal and multipotent neural cell line.
- Group II, claim(s) 5, drawn to an isolated cell or tissue derived from a multipotent neural cell.
- Group III, claim(s) 6-11, drawn to a transfected multipotent neural cell.
- Group IV, claim(s) 14-21, drawn to a method of identifying multipotent cell comprising measuring various antigens.
- Group V, claim(s) 22, drawn to a method of purifying a multipotent neural cell.
- Group VI, claim(s) 23-25 and 29-31, drawn to a method of enriching a population of multipotent fetal neural cells.
- Group VII, claim(s) 32, drawn to a method of treating a mammal having a neurological syndrome or disease comprising implanting a multipotent neural cell.

The inventions listed as Groups I-VII do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Group I is directed to a CNS immortal and multipotent neural cell line, which is the first product. However, because Major et al teach a CNS immortal and multipotent neural cell line, no special technical feature exists for Group I as defined by PCT Rule 13.2, because it does not define a contribution over the prior art. Groups II-III are drawn to structurally different products, which do not require each other for their practice and do not share the same or a corresponding technical feature. The technical features of Groups IV-VII are drawn to methods having different goals, method steps and starting materials, which do not require each other for their practice and do not share the same or a corresponding technical feature. Note that PCT Rule 13 does not provide for multiple products or methods within a single application. Because the technical feature of Group I is not a special technical feature, and because the technical features of the Group II-VII inventions are not present in the Group I claims, unity of invention is lacking.